TO STUDY THE ALLERGY DETECTION TEST AND EFFECT OF DESENSITIZATION PROCEDURE IN VARIOUS ALLERGIC DISORDERS IN BUNDELKHAND REGION

THESIS FOR
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DEEPAK SHARMA

C E R T I F I C A T E

This is to certify that the work entitled "TO STUDY THE ALLERGY DETECTION TEST AND EFFECT OF DESENSITIZATION PROCEDURE IN VARIOUS ALLERGIC DISORDERS IN BUNDELKHAND REGION" which is being submitted as a thesis for M.D.(Medicine) examination, 1992 of Bundelkhand University by DR. DEEPAK SHARMA, has been carried out in the department of Medicine, M.L.B. Medical College, Jhansi.

He has put in the necessary stay in the department as per university regulations.

Dated: 10.8.91

(R. C. Arora)
M.D., D.Sc.,
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Dated : 10.8.91

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CERTIFICATE

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ACKNOWLEDGEMENT

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M.D., D.Sc.,

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C O N T E N T S

INTRODUCTION

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Allergic diseases (asthma, allergic rhinitis and urticaria along with food allergies) are important cause of morbidity ranging from trivial discomfort to total incapacitation and abstinence from work. Many studies and surveys have been done so far to assess these diseases. According to National Ambulatory Medical Care Survey done in United States more than 14 million physician's office visits for asthma and allergic rhinitis were made in 1980, and medication was prescribed in more than 90% of the visits (Cypress, 1983).

Maternowski and Mathews (1962) in their study and Sheery and Scot (1978) in a separate study concluded that allergic diseases in the U.S. population fall in the range of 19% to 34%.

In our set up these disorders are also quite common. It is estimated that more than 10% population of India suffers from one or the other allergic disorders (Kochar, 1986). Of all the system of human body allergic disorders of respiratory system and the skin, affect about 6 to 7% of the population in India. Morbidity surveys have revealed that more than 1% of our country suffers from bronchial asthma, another 3-4% suffers from allergic colds for months at one time or another.

Term allergy originated long back . Von Pirquet coined the term in 1906. It is derived from a

Greek word Allos ergon. Allos meaning other and ergon meaning action, hence other action or altered reaction. Since then many immunologists have tended to use the term allergy for the hypersensitivity states that are deranging to the body, retaining the older term immunity for those which are basically protective.

'Atopy' is a form of clinical allergy, which is of inherited nature, patients of atopic constitution have a tendency to produce antibodies (called reagin or immunoglobulin E) in greater amounts after natural exposure to substances, which are usually harmless to normal persons. These patients have an increased risk of developing asthma, allergic rhinitis, urticaria, atopic eczema and allergic conjunctivitis.

Allergic diseases, because of their high incidence have always been of clinical interest, and all potential areas of their cure have been explored.

Williams and Menicol (1969) in their study found that 3.7% of population had regular episodes of asthma from early childhood to ten years of age. Lee et al(1976) found that 11% of population have allergic asthma at an early age. According to one study (Michael, Kalinei, Peyton Eggleston et al, 1987) approximately 9% of all patients seeking medical care at a physician do so for one of the common allergic diseases in United States.

According to another study in 40 million American with allergic diseases, 25-30 million have hay fever alone,

8.9 million suffer from asthma with or without hay fever and 11.8 million have other allergic diseases such as eczema, angioedema, urticaria, food drug or insect hypersensitivity (King & Norman, 1975). These antigen are usually derived from natural organic sources such as house dust, pollen, mold spores, insects and animal denders.

Bruce Pearson (1958) elicited that nearly 50% patients suffering from allergic diseases had family history of allergy.

IgE medication in the allergic diseases is well documented. Johnson found that 63% of patients with allergic asthma have raised IgE level in serum, however, 5% of those who do not have allergic asthma, IgE level may be found raised. Robinson (1973) endorsed the belief that asthmatic peroxysm is triggered by the hypersensitivity reaction or by mental stress. The causation of asthma may be due to hereditary asthmatic diathesis plus a specific sensitizing antigen alone or a combination of reflex nervous activity and lung damage.

When it comes to treat allergic illnesses few considerations are important, first is to confirm the immunological bases of illness and exclusion of other possible etiologies. Second is to find out the offending antigen, third and most important step is to plan treatment and to maintain the immune status which is being constructed by therapy. From time to time many approaches have been made to find out the offending allergen.

Experimental provocation of symptoms with inhaled allergen for respiratory allergies and with contactants for skin allergy is most relevant approach. But this has quantitative and qualitative difficulties and safety is often challanged. Epicutaneous and intercutaneous skin testing by a variety of non-standardized techniques prevailed until mid 60's. Introduction of RAST (Radio-allergosorbent test) in 1967 was considered as if it might replace skin test in clinical practice. Many studies have been conducted to compare skin test and RAST along with their relation to rise in IgE. It has been seen that skin prick test is equally effective when it is compared to other methods of allergy detection.

In the past 20 years most of the well designed comparative studies have shown a high correlation between skin test reactivity (STR) and serum level of specific IgE. (Kniher, Hales et al, 1981; Berg, Johansson, 1974; Eriksson N, 1977).

In 1983, American Academy of Allergy and Immunology released an official paper according to which optimally performed skin tests and RASTS both detect IgE antibody accurately and reproducibly. RAST and skin prick test yield information of semiquantitative nature, but RASTs are less sensitive than skin test. Results of both tests correlate well with allergic symptoms and sign produced by exposure to specific allergen tested. Both tests can be used as ground for instituting immunotherapy.

In the diagnosis of anaphylactic states skin test is superior, moreover results of skin test are more immediately available (45 minutes as compared to 2-3 days in RASTs). Skin test is more sensitive, faster and relatively less expensive to the patients.

Allergic diseases are quite common in our set up (Nearly 10% of patients attending medical and ENT out patient departments have one or the other type of allergic problems. Most of them seek advice multiple times as they are not relieved by routine antihistaminic and bronchodilator treatment. There is an another group of patients who have undergone some sort of ENT surgery but are not benefited and they continue to have symptoms.

In view of such problems, present study is designed to study the spectrum of allergic illnesses in Bundelkhand region and to confirm their allergic nature by skin prick test using 84 allergens. An approach is also made to know the prevalence of various allergens in environment. Further more the possible beneficial effects of immunotherapy in the management of these diseases is also taken into account.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

During the past two decades, few areas of medicine have experienced as dramatic a change in the rationale for therapy from pervasive empirism to a substantive degree of rational therapy. Allergy and clinical immunology is one of them. Basic immunological principles and mechanisms infact provide clues for the diagnosis and management of allergic diseases. Immune system takes into account those mechanisms which conter specffic immunity. However, other nonspecific defense mechanisms like muco-ciliary epithelium of respiratory tract or proteolytic enzymes of external secretions, also exist in the body, which help to protect body.

Specific immunity implies the acquisition of a biologic response in which circulating antibodies or lymphocytes interact with a unique molecular, or a very restricted range of molecular configurations, presented to them. The molecules that elicit the immune response are called antigen which usually are high molecular weight proteins, carbohydrates or nuclic acids. Out of these, those that elicit an allergic or hypersensitivity response are called allergens.

ONTOGENY OF IMMUNE SYSTEM

The immune system arises from developing lymphoid tissue during embryogenesis. The lymphoid organs are

divided into two categories - central and peripheral. In humans the central lymphoid organ is the thymus. It gives rise to two major populations of lymphocytes mediating specific immunity.

There are B cells (Bursadependent) which are involved in humoral or antibody mediated immunity and T cells (Thymus dependent) involved in cell mediated immunity.

Thymus is rich in T cells, arising from a common lymphoid stem cell migrating to the thymus (Bryant, 1974). In thymus their differentiation is stimulated by a humoral factor produced by thymic epithelium, termed as thymopoietin or thymosin (Goldstein, Hooper et al, 1974; Wara et al, 1975 and Scheinberg et al, 1976).

T cells migrate from the thymus by way of the blood stream and lymphatics to populate the peripheral lymphoid organs i.e. the lymph nodes, spleen, bone marrow, tonsils and gut associated lymphoid system (Hall, 1974).

The division of lymphocytes into T and B cells was first described in chicken (Cooper, Peterson et al; Motica, 1966).

B cell precursors are demonstrable in the mammalian fetal liver and in adult bone marrow (Gathingswer, Lawton et al, 1977). Migration of B cells to the peripheral lymphoid organs also occur (Pearl, Vogler, Okos et al, 1978).

A third lymphoid cell evolving from the central stem cell line during this period is the monocyte or in it's mature form macrophage. Over past several years it has been recognised that interaction of macrophages with T and B cells is important in the initiation of the immune response and it's regulation (Pierce, Kapp, 1978).

HUMORAL IMMUNITY

Stimulation of production of specific antibodies depends upon the nature of antigen antibody activity in humans resides in five major classes of globulins. These immunoglobulins classes are termed IgM,,IgA, IgD, IgE and IgG. Each immunoglobulin class appears to be synthesized by a separate B cells subclass. It has been recognised that for maximal B cell, IgM and IgG primary responses, presence of T cells is required (Katz, Benacessaf, 1972). This subpopulation of T cells is known as HELPER T CELLS (Friedman, 1975; Graves, 1973). In contrast to the majority which are T dependent antigens, there are few antigens which do not require mediation by T cells. These are called as T independent antigens (Moller, 1973). Along with interaction of B and T lymphocytes, macrophages play a vital role. Initially antigenic proteins bind to macrophage before their recognition by T lymphocytes (Basten, Mitchell, 1976).

Macrophages process or degrade the antigen and then the antigen is combined with a product of genes which

are linked to the histocompatibility complex (MHC) of the species. This gene product is called Ia or immune response associated, presumably coded for by a corresponding Ir or immune response gene. The combination of processed antigen and Ia is then presented to T cell for immune recognition and stimulation of T cell to helper activity or effector activity (Benacessaf B and Germain RN).

The nature of receptor on the T cell surface which recognize specific antigen is still open to the discussion (Saligmann M, Preud Homme JL et al). In contrast, B lymphocytes have readily identifiable IgD and IgM monomer present on their cell membrane (Saligmann N et al, Franklin EC, 1978).

REGULATION OF ANTIBODY SYNTHESIS

It is known that following interaction of macrophage, B lymphocytes undergo blastogenesis and are transformed into a mature plasma cells, which synthesize immunoglobulin. Many regulatory mechanisms, however, operate over this.

IgM - B cells are suppressed by circulating IgG antibody directed against the same antigenic specificity (Sercurz, Williamson and Fox, 1974). Furthermore suppressor T cells exert a regulatory effect. There is growing evidence that yet another T cell population may exist, generating an opposing amplifier signal. Amplifier and suppressor T cells appear to generate complementary

effects to keep the degree of B cell activity appropriate to antigenic stimulation (Benacessaf, 1978). Macrophages also exert modulatory influence on B cell biosynthesis mediated by elaboration of so called monokine which enhances antibody formation (Dimitrin and Fanci, 1978).

IMMUNOGLOBULINS

Following types of immunoglobulins exist.

IgG

This is the major protective antibody of intravascular compartment. It's concentration usually increases with repeated antigenic stimulation. It's molecular weight is 150,000 Dalton with a half life of 23.0 days. Adult serum concentration is 600-1800 mg/dl.

IgM

It is found in lesser concentration than IgG. This is earliest antibody produced in most primary immune response. It has a molecular weight of 900,000. It's serum concentration is 60-250 mg/dl.

IgA

It comprises about 20% of serum immunoglobulins. It's important role is as protective antibody of the external and internal secretion. It is present in large amounts in saliva, colostrum, lacrimal and nasal secretions. It has a molecular weight of 170,000 Daltons. It's serum concentration is 90-450 mg/dl.

IgD

It is found free in circulation in low concentration. It serves as an antigen receptor or recognition site on the uncommited B cell. It's molecular weight is 184,000. It's serum concentration is 0-14 mg/dl.

IgE

IgE has been shown to be the principal mediator of immediate (type I) hypersensitivity reactions (Norman, PS). IgE binds to tissue mast cells and basophils. This cell bound complex then causes degranulation of basophils on combining with allergen.With the result histamine and other mediators of type I reaction are released(Beaven MA). Its molecular weight is 190,000. It is present in lowest concentration (10-406 IU/ml). IgE concentrations are generally higher in the allergic population although there is considerable overlapping with nonatopics(Horburger,1978).

CELL MEDIATED IMMUNITY

The parallel mechanism of immune recognition and immune regulation are analogous in humoral and cell mediated immunity (Parker CW). However, immune reaction in CMI (cell mediated immunity) is brought about by sensitized lymphocyte, rather than a free antibody molecule. The development of antigen specific T lymphocytes is dependent on interaction of macrophage and T cell. After antigen recognition a proliferative phase insues,morphologically characterised by production of lymphoblasts

1. Memory T cells : These cells are fairly long lived and are important in maintaining immunologic memory of previously encountered antigens (Benner R, Von Ondenarm A et al, 1977).
2. Suppressor T cells : Both immunoglobulin class specific and antigen specific suppressor T lymphocytes have role in antibody production. They have role in regulation of effector cell's response in CMI. They also establish tolerance to self antigen (Kapp JA, Pierce CW et al, 1968).
3. Amplifier T cells : They act in opposition to suppressor T cells in regulation of B cell activity. It is however, not clear that an analogous population is operative in regulation of CMI.
4. Effector T cells : They on contact with antigen create the molecular cellular and clinical manifestation of CMI reaction.

Macrophage which is not a T cell. Can also exert a regulatory effect on effector cell activity in CMI. This activity is different than it's role in initiation of antigen specific immune responsiveness. Effector T cells are induced to perform their functions by elaboration of soluble mediators called lymphokines (JJ Oppenheim), which are produced by antigen specific memory T cells upon contact with antigen.

5. Killer or K cells : These cells bring about lysis. They are infact the sensitized effector T lymphocytes. Binding of K cells to target cells is a pre-requisite for lysis.

CLASSIFICATION OF HYPERSENSITIVITY REACTIONS

Gell and Coomb classified hypersensitivity reactions. Several modifications however have been proposed to the Gell and Coomb classification system (Sell, 1975). Many immunological processes incorporate more than one type of hypersensitivity reaction.

1. Type I (Anaphylactic) Reaction:

This type of reaction is also called immediate type hypersensitivity or reaginic hypersensitivity. Clinical condition as extrinsic bronchial asthma, allergic rhinitis, urticaria, food allergies and reaction to stinging insects and systemic anaphylaxis, all are mediated by this type of immune reaction. Immunoglobulins which mediate this reaction are called reagin. Ishizaka and Ishizaka (1970) have shown that IgE possess the classic characteristics of reagin. IgE does not cross placental barrier. This can freely circulate in blood or may remain bound to basophils and/or mast cells. Anaphylactic reaction is brought about by many mediators. Histamine, SRS-A, serotonin, eosinophilic chemotactic factor of anaphylaxis, platelet activating factor, prostaglandin are all mediators that potentially can give rise to hypersensitivity

capillary permeability and contraction of smooth muscles.

Type II (Cytotoxic) Reaction

These reactions are also termed as complement dependent cytotoxicity. Complement system is also required to mediate type III or toxic complex reaction along with this type.

In type II reaction this system works when cell bound antibodies combine with antigen and in type III reactions it works when cell bound antibody and antigen complex has settled down at the place of reaction. Complement system is composed of serum protein which when react in combination have the capacity to cause cell lysis.

Ehrlich and Bordet put the guidelines of events involved in cell lysis.

Complement system involves two major subsystems.

1. Classical pathway.
2. Alternate pathway.

In the activation of complement system there is:

1. Sequential activation of inactive precursors. (zymogenes).
2. Activation of increasing number of molecules in subsequent steps of the sequence (Cascade).
3. Amplification of propogation of inflammation by product of activation.

Type II reactions have two subgroups.

In one complement fixing antibody is directed against endogenous antigenic determinant of cell membranes, example - Transfusion reactions.

In second group the antigenic determinant is exogenously introduced and then binds to the cell membrane, example. Haemolytic disease of new born and neonatal thrombocytopenic purpura.

3. Type III or Toxic Complex Reaction

These reactions are also referred as immune complex hypersensitivity reactions. Clinical conditions that are mediated by toxic complex reaction include Arthus reaction, clinical serum sickness and certain glomerulonephritides. Complexes made of cell - antibody - antigen settle at the place of reaction, and through activation of complement system damage is produced.

4. Type IV or Cellular Hypersensitivity

This is also called delayed hypersensitivity as a delay of 24 to 72 hours occurs in the initiation of reaction. Delayed hypersensitivity is not mediated by circulating antibodies, but is mediated by antigen specific sensitized lymphocytes. Tuberculin hypersensitivity contact dermatitis, allograft rejection, Graft versus host disease as a sequele to bone marrow transplantation are conditions which involve type III reaction.

Richet and Porter had described the development of anaphylaxis in dogs. In 1922 Prausnitz and Kustner

described the tranfer of immediate hypersensitivity from an affected individual to a normal individual by serum, and the test employed for the detection of presence of this type of antibodies was termed as P-K test.

Medical evaluation for atopic diseases like allergic asthma, allergic rhinitis, urticaria traditionally has consisted of three parts :

1. History.
2. Physical examination and
3. Skin testing with appropriate allergen.

Different techniques of performing allergy skin test are well known (Mangi RJ) and variability between commercial allergen also is well documented (Ford DW, et al and Tunginger JW).

There are other variable as well which also affect the skin test interpretation. They are :

1. Storage, age and concentration of extracts (Yunginger JW, Gleich GJ, 1978).
2. Instrument used to apply test (Sheldon JW et al).
3. Criteria for grading result of skin test(Patterson R).
4. Time of day (Lee RE et al).
5. Area of body where test is applied (Voorhorst R.).
6. Subjective evaluation of skin test reactivity by different personnel (Aas K.).

Skin prick test for allergy detection involves allergen induced wheel and erythema response which was firstly described by Blackley.

In 1954 Herzheimer et al studied the evaluation of skin test in respiratory allergy.

Holman et al studied skin test and bronchial challange test correlation and concluded that it is the skin test with provides important information when considering immunotherapy.

Brown et al (1979) studied the respiratory allergy skin test reactivity and serum IgE relationship in a population.

From time to time the safety , cost and effectiveness of skin allergy test has been studied. When compared to skin test other tests are expensive and less sensitive (Adkinson NF).

Coca and Grove did extensive studies of the skin sensitivity factor from sera of patients with ragweed hay fever. Gleich and co-workers have been able to define the natural rise and fall in ragweed specific IgE over a period of one year. Ishizaka and Ishizaka using RAST technology had made observation that there is rise in IgE after a pollen season.

Although RAST and other IgE measuring technology have added to the knowledge, thest tests at present do not replace simple skin testing with the allergen, moreover skin test provides important information when treatment is being planned (Gleich et al).

Most testing is dependent on the production of an allergic reaction by the intentional exposure of the

are used in clinical practice.

With the Scratch test antigen is applied to a superficial scratch that penetrates the outer cornified area of skin. In prick test skin is pricked by a needle through a drop of antigen solution. Intercutaneous test is performed by injecting a small amount of antigen in the superficial layers of skin. The antigens used may vary because of the prevalence of particular antigens is a particular geographical location. Results of SPT are often compared with those obtained by other methods.

Juhlin and Dannfelt have failed to obtain a positive bronchial response to any antigen when the skin tests have been negative on the other hand Colldahl in his study has found positive bronchial reaction in patients who had negative skin test.

SPECTRUM OF ILLNESS

1. Allergic Rhinitis

Seasonal allergic rhinitis is a specific allergic reaction of the nasal mucosa principally to pollens, characterised mainly by watery rhinorrhoea, nasal congestion, sneezing, itching of eyes, nose and throat though there is no fever essentially still this condition is also referred as Hay fever. Though it's incidence is greater among children and young adults, no age, however, is exempt. Cooke and Vandenveer showed the role of heredity in etiology. Tennensawm (1970) also endorsed their findings.

Phillips has shown that individual requires two or more seasons of exposure before exhibiting clinical manifestation of disease.

Smith reported that 80% of patients develop their symptoms before the age of 30 years. Cell bound IgE antibodies in the response of antigenic stimulation, cause release of mediators of immune reaction and bring about manifestations of disease (Kaliner M, Wasserman SI and Austin KF, 1973).

Connell (1969) defined that there may occur inflammation following the acute phase reaction due to hyper-reactivity of allergic nose to a variety of non-specific stimuli such as cigarette smoke, strong odours, air pollution and climate changes.

Nasal provocation testing to detect the condition with suspected allergens is of research value as there are difficulties and so it's clinical usefulness is limited (Solomer and Mclean, 1983). According to Michael Kaliner (1987) skin testing with potent antigenic preparations and positive and negative control substances remains the most revealing procedure in diagnosing specific allergic factors associated with allergic rhinitis.

Some patients develop shortness of breath due to allergic tracheobronchitis. This may be a warning signal of possible development of allergic asthma. The characteristic of symptom complex is that it appears at a certain time of year and its periodicity or frequency.

Mygind and Lowenstein (1982) have shown that atopic skin test positive rate is 35% in healthy population. Aas has proved that immediate skin tests for some allergens are equally reliable as RAST.

Perenial (Nonseasonal) Allergic Rhinitis:

In this condition there is intermittent or continuous nasal symptoms due to allergic reaction without seasonal variation. There is usually a chronic antigenic challange resulting in recurring almost continuous symptoms. Major perenial allergens include house dust, feathers, mold, animal denders. This may be due to occupational allergens, example, in flour industry workers (studied by Schwartz M), Detergent workers (studied by New house M) and wood workers (studied by Sosman AJ) diseases occur due to hypersensitivity to these things.

Alteration of normal physiology and symptom complex of this condition are similar to seasonal allergic rhinitis but are less severe and more constant.

Vasomotor Rhinitis

It is associated with an altered vasomotor control resulting in the development of chronic nasal congestion. This is nonimmunologic, non infectious. Many nonspecific stimuli act on the autonomic nerves resulting in reflex changes in the nasal mucosa.

Holmes, Goodell and co-workers have shown that emotional stimuli trigger nasal obstruction and rhinorrhoea.

may induce similar nasal changes. Most patients with this condition show no reaction to skin test, but a small proportion may show a positive result which is incidental and does not correlate with clinical history.

Infectious Rhinitis

In this form there is fever and malaise along with local symptoms. Discharge is purulent, each attack may last for 1-2 weeks.

Hyperplastic Rhinitis

In this condition purulent sinusitis superimposes upon allergic rhinitis, there is marked mucosal oedema.

Kern and Schenic have shown that nasal polyps occur in uncontrolled allergic rhinitis.

Difference between Allergic and Nonallergic(vasomotor) Rhinitis

	Symptoms	Allergic	Vasomotor
1.	Seasonal variation	Present	Absent
2.	Nasal, ocular, palatal itching.	Present	Rarely
3.	Rhinorrhoea	Watery	Mucoid
4.	Pale nasal mucosa	Present	Absent
5.	Collateral allergy	Common	Unusual
6.	Nasal polyp	Occasional	Occasional
7.	Family history of allergy	Present	Absent
8.	Nasal secretion eosinophilic smear	Positive	Rarely positive
9.	Skin test reactivity	Almost always positive.	Negative

2. Allergic Asthma

Word 'Asthma' is derived from a Greek word meaning short drawn breath . There is no universally accepted definition of Asthma. It may be regarded as diffuse obstructive lung disease with hyperreactivity of the airways to variety of stimuli and high degree of reversibility of obstructive process which may occur either spontaneously or as a result of treatment. Irritability or hyper-reactivity of airways is manifested as broncho-constriction following exercise, natural exposure to strong odour, irritant fumes, tobacco, smoke, cold air, or intentional exposures to parasympathomimetic agents. Polygenic or multifactorial determinants control the inheritance of asthma. Lability of broncho-constriction with exercise has been found concordant in idential twins but not in dizygotic twins. Brnchial lability in response to exercise testing also has been demonstrated in healthy relatives of asthmatic children.

Etiology

Asthma is a complex disorder involving immuno-logic, autonomic, biochemical, infective, endocrinal and psychologic factors, in varying degree in different indi-viduals. Neural and humoral factors govern the diameter of airways, Neural broncho-constrictor activity is mediated through the cholinergic portions of autonomic nervous system. Vogal sensory ending initiates end stimulate bronchial smooth muscle contraction. On the

neural bronchodilator side a non adrenergic inhibitory system is found like that of ganglionic cell of myenteric plexus. Humoral factors of bronchodilation include catecholamines which act on beta adrenergic receptor to produce relaxation of bronchial smooth muscle. When humoral substances such as histamine and SRS A are released though immunologically mediated reaction, they produce broncho constriction either by direct action on smooth muscle or stimulation by vegal sensory receptors.

Szentivanji's theory considers asthma, to be due essentially to abnormal beta adrenergic receptor adenylate cyclase function with decreased adrenergic responsiveness. The recent report of decrease beta adrenergic receptor on leucocyte of nonadrenergic drug treated asthmatics may provide the morphological basis for the observed hyporesponsiveness to beta agonist. Alternatively, increased cholinergic activity in the airway has been proposed as fundamental defect in asthma, perhaps due to some intrinsic or acquired abnormality in irritant receptors which have been seen to lower threshold for response to stimulation. In individual patient a number of factors generally contribute in varying degree to the activity of asthmatic process.

Clinical Manifestations

The onset of attack is usually acute through it may be insidious. There is cough which sounds light and is nonproductive early in the course. Wheezing tachypnoea and

prolonged expiration are present. There may be use of accessory muscles of respiration and hyperinflation of chest. Abdominal pain may be present depending upon the severity and duration of illness. Recurrent episodes and precipitation of attack on exercise is characteristical.

Rackman (1963) divided asthma into extrinsic asthma which is caused by allergen or external factors and intrinsic asthma caused by non allergic factors. Differences between two types are :

Symptoms	Extrinsic	Intrinsic
Age of onset	3-35 years	⟨3 and ⟩35 years.
Symptoms	Seasonal and perenial	Increased in winter increased by cold air, infection, pollution.
Mucous	Clear and foamy	Thick and white or colourless.
Atopy	+ve	Absent
Skin test	+ve	Negative
Serum IgE	High	Normal
Response to therapy	Good response to immunotherapy and bronchodilators.	Poor response to therapy

Clinically asthma can further be described as spamotic - If isolated attack occurs with longer symptoms free intervals.

Continuous - When some amount of wheezing is present almost everyday.

Intractable : When symptoms are constant and refractory to treatment.

Status asthmaticus : When little or no response is obtained to bronchodilators as patients respiratory metabolism is greatly imbalanced.

There is a special category of nonantigenic asthma. This is induced by the ingestion of asprin, as described by Samter and Beer. Skin test to asprin are always negative in these patients.

3. Urticaria

It consist of raised, erythematous, skin lesions which are marked by pruritis. Angioedema is characterized by asymetrical swelling of tissue. This is like urticaria but involves deeper tissue. Urticaria and angioedema may occur together.

Mathews concluded that nearly 20% population at some time in life suffers some form of urticaria. Acute urticaria persists less than 6 weeks while episodes which last more than 6-8 weeks are referred as chronic urticaria. Pathogenesis is being mediated by histamine release.

Triple response observed by Lewis, is consist of erythema due to capillary and vascular dilatation, oedema due to increased capillary permeability and flare due to axon reflex. Intercutaneous injection of histamine inflicts similar type of response along with pruritis implicating that histamine mediates the urticarial response.

Urticaria occurs due to IgE mediated immediate hypersensitivity induced by antigen and being brought about by histamine release from mast cell via complement eosinophil chemotactic factor and platelet activating factor. Direct histamine release occurs with some drugs and chemicals. Plasma Kinin system may play a role in causation of urticaria by producing bradykinin which is known to increase capillary permeability. This system is activated by negatively charged surfaces, collagen vascular basement membrane or endotoxin. Fever, heat, alcohol intake, exercise, emotional stress, premenstrual or postmenstrual status, hyperthyroidism, adrenergic and cholinergic agents modulate mediator release from mast cells and basophil and may play a role in causation of urticaria.

Classification of Urticaria

Following are the types of urticaria.

1. Dermographism.
2. Physical urticaria.
3. Hereditary urticaria.
4. Papular urticaria.
5. Urticaria pigmentosa.
6. Miscellaneous (caused by drugs, food, systemic vasculitis, infections, serum sickness, psychogenic cause insect bite and transfusion reaction).

4. Food Allergy

Dees reported incidence of this in children as 3%. Fries after his study concluded that incidence decreases with the advancing age. According to Golberg, food allergy causes variety of cutaneous, gastroentestinal and respiratory manifestations. Urticaria and angioedema is most common. The clinical manifestation of food allergy usually result from type I hypersensitivity (Golbert).

Chua et al (1976) have shown that positive cutaneous tests neither establish nor confirm a definite diagnosis of clinically significant food allergy. May (1976) also had similar opinion. Both Chua et al and May demonstrated presence of reaginic antibodies in patients who had negative prick test. According to other study skin tests were negative in only 24% of patients who had positive history of food allergy.

ALLERGEN IMMUNOTHERAPY

Immunotherapy refers to the treatment in which patient is given injections of antigenic material to which they are sensitive.

Freeman and Noon (1911) firstly treated grass pollen sensitive patients with injection of extract of grass pollen. They treated 18 patients who had sensitivity to grass pollen and 16 patients had beneficial effects.

Cook conducted similar studies. In his study 114 patients were treated with pollen immunization for ragweed allergy and nearly half of them had beneficial

effects.

Since 1949, many studies have been conducted using immmunotherapy to the patients who had allergic disorders (Fontana, Holt et al, 1966). Lowel and Franklin (1965) conducted double blind study of the effectiveness of immunotherapy for ragweed hay fever. Melam, Pruzanbky and Patterson et al (1971) also showed beneficial effects of injection immunotherapy. Sadan, Rhyme and Mellits investigated immunotherapeutic response in pollinosis in children.

Frankland and Augustin have reported that 94% of their patients who received immunotherapy for asthma and rhinitis had improvement in their symptoms.

Brown (1949) conducted one of the initial studies concerning immunotherapy to house dust sensitive patients. He showed 78% of patients had improvement in their symptoms.

Ass (1971) found that 87% of 52 asthmatic patients (asthmatic children) with house dust reactivity had a significant reduction in bronchial reactivity after treatment with house dust immunotherapy.

Taylor et al (1978) have shown improvement in symptoms in asthmatic patients sensitive to cat dander after treatment with a very potent cat pelt vaccine.

Though many studies have shown beneficial effects some workers have reported other way. Bruce et al treated a group of patients of allergic asthma (sensitive to

ragweed) and there was no improvement in symptoms after treatment. Causes of failure could be improper detection of antigen, failure to include other antigen to which patients were sensitive or could be due to low dosage of antigen given.

The safety of immunotherapy has also been challanged from time to time.

Kohler in his study found development of Arteritis in patients who were undergoing immunotherapy. Kohler and Phanupak have shown that 5 outnof 19 patients treated by immunotherapy developed polyarteritis nodosa.

Levinson, Summers, Lawley et al (1978) compared a group of atopic patients receiving immunotherapy for five years with those who were not receiving any therapy. The treated group did not show an increased incidence of auto-immune collagen vascular or lymphoproliferative disease.

Lichenstein,,Norman and Winhenwerder (1968) have shown that immunotherapy leads to an increase in IgG blocking antibody titres. These antibodies block histamine release by combining with antigen before it reacts with IgE antibodies fixed to mast cells. The rise in titre is dose dependent.

Starr and Weinstock (1970) have shown that higher titres result in less symptomatic patients. There is a decrease in sensitivity of leucocytes to histamine release to antigen following immunotherapy.

According to Sherman, Stull and Cooke there is a decline in serum IgE directed against specific antigens in patients receiving immunotherapy.

Levy (1971) found that there is also a decrease in the post season rise in IgE directed against specific antigens in patients receiving immunotherapy.

By immunotherapy IgE reduction is produced by :

1. Induction of suppressor mechanisms within the allergic individuals to reduce the production of IgE.
2. Induction of specific immunologic tolerance in IgE precursor B lymphocytes which are precursors cells of IgE producing plasma cells.

While immunotherapy is carried out for all sorts of allergic disorder, immunotherapy is not recommended for treatment of food allergy. If food allergy is present dietary exclusion of foods is the treatment of choice.

AIMS OF STUDY

AIMS OF STUDY

1. To study the spectrum of various allergic disorders prevalent in the Bundelkhand region and confirm their allergic etiology.

2. To find out the prevalence of various allergens and which one is commonest.

3. To evaluate the effect of immunotherapy in the management of these disorders.

MATERIAL AND METHODS

MATERIAL AND METHODS

Place of work : Department of Medicine,
M.L.B. Medical College,
Jhansi (UP).

SELECTION OF CASES

Present study comprised of the patients having allergic diseases - allergic asthma, allergic rhinitis, urticaria, food allergy. Selection of cases has been done from patients attending medical and ENT out patients department and from patients admitted in medical wards.

Diagnosis was based on detailed history, clinical examination and relevant investigations. Patients of both the sexes and of age ranging from 8 to 66 years were included. Cases belonging to various socio-economic strata and occupation were included in the study.

Prior to subjecting patients to skin prick test, they were asked to stop antihistaminics and steroids at least five days before test, which they were taking. No alteration in their diet, place of work and surroundings were made. Following informations were filled in predesigned proforma (Annexure - I).

HISTORY

History of present illness was outlined on complaints and their duration, age at which the symptoms first appeared. Severity and frequency of symptoms were noted. Relation of occurrence of symptoms with season,

particular months, hour of day, and place (whether at home or at the place of work) were outlined. Any recent change in residence or occupation was noted. History of any sort of animal contact was also asked for.

Any food components after intake of which symptoms used to occur were also asked.

Past history included similar complaints, if present in the past. History of worm infestation, any other medical illness (tuberculosis, upper respiratory tract infection) was recorded.

HISTORY OF TREATMENT

This included any drug treatment which patients took. History of any operation (nose or throat operations) was also asked for.

FAMILY HISTORY

Thorough clinical, general examination and examination of respiratory, gastrointestinal, cardiovascular and central nervous system was done in each case. In the cases of allergic rhinitis local examination of nose (Rhinoscopy) and throat was done.

INVESTIGATIONS

The following investigations were carried out :

1. Total and differential leucocyte count.
2. Haemogram, ESR.

3. Absolute eosinophil count (AEC)

AEC = TLC X percentage of Eosinophils/100.

4. Chest skiagram (to exclude other chest diseases).

5. Stool examination (to exclude TPE).

6. X-ray PNS to exclude sinusitis.

7. Ratio of forced expiratory volume in one second and total vital capacity by Spirometry.

8. Eosinophil count in various secretions, if the clinical condition requires.

ALLERGENS

Desensol (supplied by E. Merck India Ltd.) Prick test solutions containing Aqueous allergen extracts were used. The extracts contain 50% glycerol and are preserved in 0.4% phenol. The range of prick test solution used is mentioned in Annexure-II.

METHOD OF SKIN PRICK TEST (SPT)

The most suitable site for skin testing is the flexor aspect of forearm. If multiple allergens are to be tested in one sitting three rows can be made which are atleast 3 cm apart. To avoid difficulty in reading results hairy skin is to be prepared.

The skin is first marked using a felt tip pen. Now one drop of each allergens which are to be tested are put with the tip of plastic knob attached to the cap of desensol bottle. The negative control (saline) is

placed near the top of the arm followed by allergen extracts, usually with the house dust mite extract at the lower end, before the final positive control solution (Histamine). The test sites are kept 4 cm apart.

A sterile lancet is introduced subcutaneously at an acute angle to the skin and shallow lift is made. The lancet is raised for a second before the skin is released. This is repeated for each drop of solution. Lancet is carefully wiped of using cotton wool before using for each solution. Any excess solution remaining on the skin after the prick has been made, is removed by placing a paper tissue over the arm for a moment or two.

The results are read after 20 minutes when positive reaction will appear as an induration surrounded by wheal and flare. Any wheal produced by the negative control must be subtracted from any reactions produced by other allergens before they are assessed. Where both the wheal and flare are only very small that is, the reaction is only mild. This is recorded as (+) against the particular allergen. Where there was a larger reaction but not as large as the positive control the reaction was recorded as (++). Where reaction is similar to or greater than the positive control (Histamine), (+++) is recorded against the particular allergen (Criteria : Desensol booklet).

Alternative criteria to read prick test result has been proposed by Kochar AS, which is as follows :

Reaction	Symbol	Criteria
Negative	(-)	No reaction or equal to control.
One plus	(+)	Erythema $\angle$21 mm in diameter.
Two plus	(++)	Erythema $\geq$21 mm with no wheal.
Three plus	(+++)	Wheal with surrounding erythema.
Four plus	(++++)	Wheal with pseudopods and surrounding erythema.

When a permanent record of the skin test reaction is required, the wheals can be closely encircled by a felt tip ped and a piece of clear adhesive tape is applied to the test site. Thus an image of the reaction can be taken on the tape which can then be placed on patients record card.

Any contraindications for the test are not documented, except when there is history of any anaphylactic reaction in that case histamine is injected with caution. Blood should not be drawn during testing. These solutions are not used for intradermal testing as per manufacturer's advice.

Adverse reactions are rare, large local reactions if occur normally subside in short time. In unlikely event of a severe general reaction, a tourniquet is applied to the upper arm proximal to the site of skin test that has caused the reaction, and 0.3 ml of adrenaline injection (1:1000) is injected around and beneath the site of test and 0.3 ml of such solution is injected subcutaneously.

PROCEDURE OF IMMUNOTHERAPY

This is performed to hyposensitize those patients who have been shown to be sensitive to allergens as a result of case history and skin prick testing.

Desensol aqueous allergen extracts are used for specific hyposensitization. They are prepared from different allergenic materials of the human environment. Phenol (0.4%) is added as preservative. The extracts are standardized according to the weight : volume ratio of native material to the extraction fluid (for example - 1 + 99 = 1% w/v).

The composition of each treatment set is determined from the case history and reaction observed after skin tests. Thus each treatment set is individually formulated.

Initial treatment set is consist of 4 vials of 4.5 ml each.

Strength 1 : 1 + 24999 (0.004% w/v).

Strength 2 : 1 + 2499 (0.04% w/v).

Strength 3 : 1 + 249 (0.4% w/v).

Strength 4 : 1 + 49 (2% w/v).

If person is sensitive to mite or insect, A ten fold dilution as compared to above strength is used.

Maintenance treatment set of one vial of 4.5 ml containing extract of above mentioned strength 4 is used.

ADMINISTRATION AND DOSAGE

Aquous allergen extracts are rapidly absorbed after injection. Course of hyposensitization treatment is given in quick succession and dose is slightly increased each time. The interval between the two successive injections is two-three days. It is never more than 7 days. In tailoring dosage individual tolerance is also seen. If there has been a gap of more than 7 days between two injections, the dose given at next injection is not increased. In case of maintenance course, the initial schedule is repeated before restarting maintenance therapy.

Dosage scheme is shown in Annexure - III.

PRECAUTIONS

1. Injections are given in sterile condition. Patients must not have heavy meals before and should not perform heavy exercise after injection.

2. Injections are given at the extensor surface of upper arm 3 inches above olecranon as tourniquet can easily be applied.

3. Injections are never given I/V and patients are watched for ½ an hour after injection.

4. Every course of hyposensitization treatment is initiated with the lowest dose of the lowest concentration.

5. Patients who are sensitive to seasonal allergens the injections are given preseasonally and course is completed before that particular allergen becomes airborne. For perenial allergens course may be commenced at any time of year.

6. Maintenance therapy for perenial allergens is consist of repeating the top dose achieved at seven day intervals. An attempt is made to extend the injection interval to 10-20 days. This schedule may be followed for one year.

Where seasonal allergens are involved it is recommended that hyposensitization be started sufficiently before the season and the schedule should be carried out preseasonally for three successive years.

7. Immunotherapy is not instituted in acute infections, acute severe asthma and pregnancy.

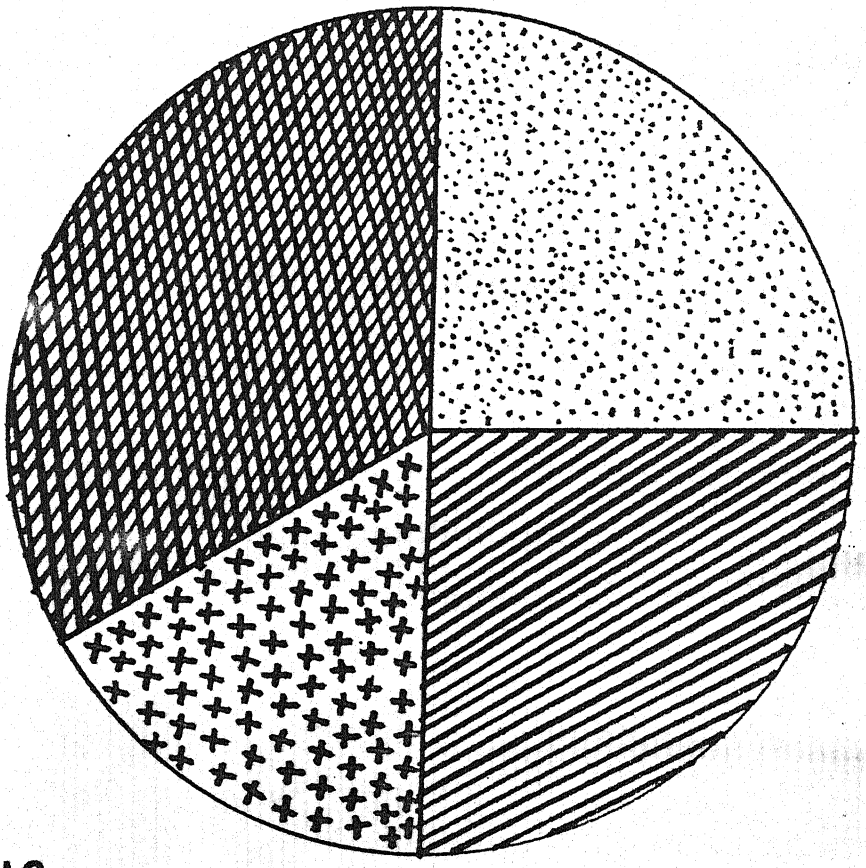
8. Recommended emergency kit should have :

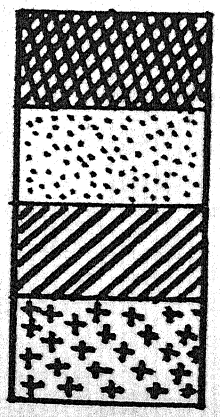
a. Tourniquet
b. Adrenaline
c. Hydrocortisone.
d. Oxygen mask.
e. Injectable antihistaminics
f. Aminophylline ampoules
g. Plasma expender(Dextran)

OBSERVATIONS

Pie-Diagram showing incidence of various allegic disorders in Bundelkhand region.

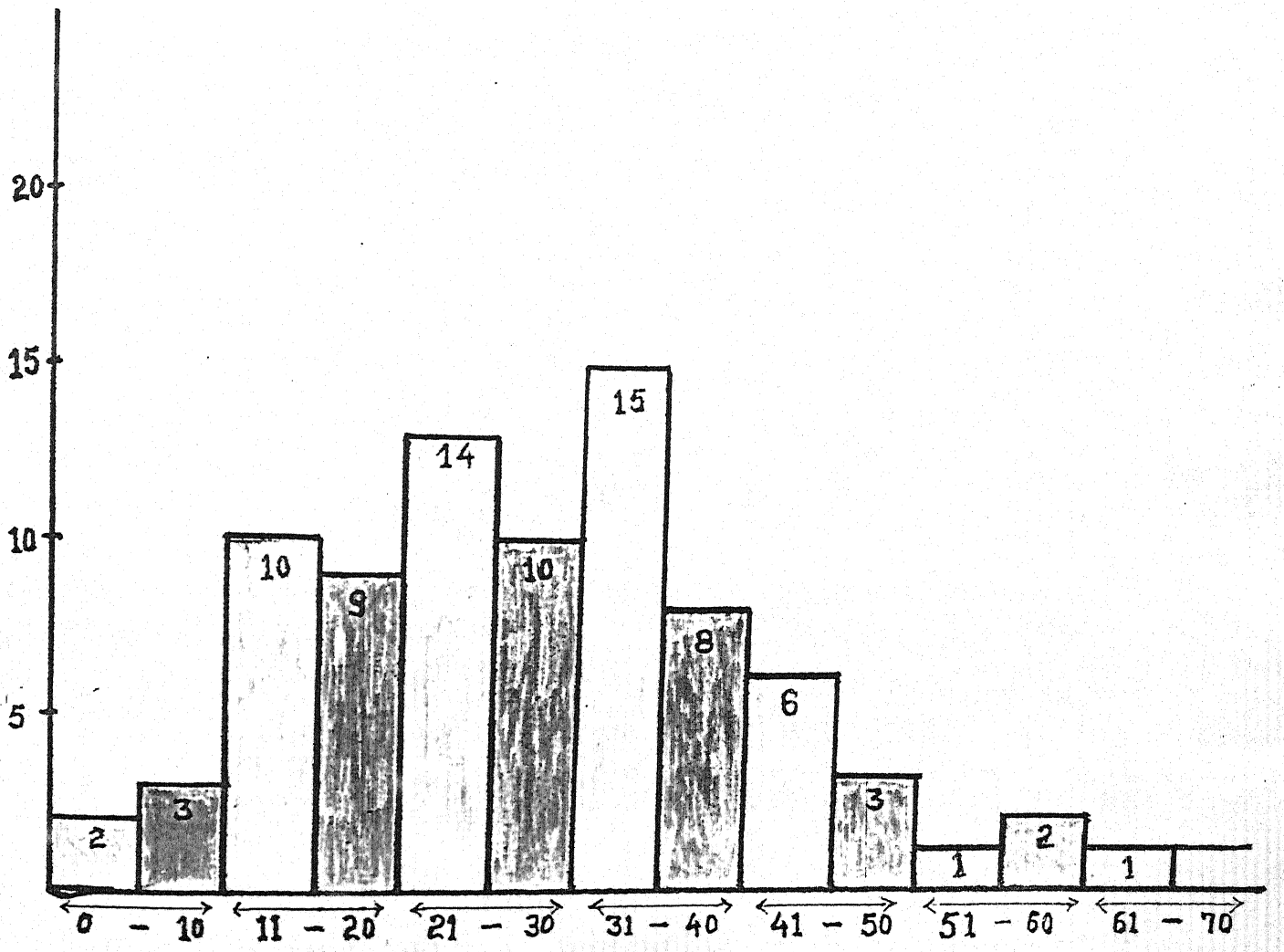
June 1990-May 9

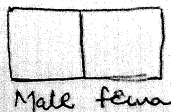




RHINITIS
ASTHMA
MIXED
URTICARIA

Bar diagram showing distribution of cases in relation to age and sex.





OBSERVATIONS

The present study was conducted in the department of Medicine, M.L.B. Medical College, Hospital, Jhansi during the period of one year from June, 1990 to May, 1991 to analyse the spectrum of various allergic disorders (Allergic rhinitis, allergic asthma, urticaria). Cases were selected from patients attending medical OPD, ENT OPD and patients admitted in medical wards.

Eighty four patients were included in the study. Out of these, 49 were males and 35 were females. Age range was from 8-66 years. Mean age for males was 30.24±30.39 years and that for females was 28±30.27 years.

TABLE 1 : Showing the characteristics of cases.

Characteristics		No.of cases
OCCUPATION		
	Students	19
	Medicose	7
	Housewives	23
	Business persons	6
	Outdoor workers	12
	Office workers	12
	Miscellaneous	5
PHYSICAL ACTIVITY		
	Sedentary	52
	Active	32
ONSET OF SYMPTOMS AFTER RECENT CHANGE IN		
	Occupation	16
	Residence	21
HOME SET UP:	Rural	27
	Urban	57
DIETARY HABITS :	Vegetarian	49
	Non-vegetarian	35

Table 1 shows that subjects belonged to various categories and had different general characteristics. Out of 24 students including 5 medical students 9 had the onset of symptoms of allergic disease after the change in occupation. 2 business men changed their occupation. Four outdoor workers changed their occupation, while one office worker had recent change in occupation. This signifies that change of occupation might have led to the exposure of that individual to a particular allergen.

Out of 21 persons who changed their residence before the onset of allergic symptoms included 9 students, 9 housewives, 2 field workers and one individual who also had changed his occupation.

TABLE 2 : Showing the distribution of cases according to age and sex.

Age groups (years)	Male	Female	Total
0 - 10	2	3	5
11 - 20	10	9	19
21 - 30	14	10	24
31 - 40	15	8	23
41 - 50	6	3	9
51 - 60	1	2	3
61 - 70	1	-	1
TOTAL	49	35	84

Table 2 shows the distribution of cases according to their age and sex. Youngest subject was

8 years old while eldest subject aged 66 years. Maximum cases were in their 3rd and 4th decade of life.

These patients had their onset of symptoms not from the birth suggesting their extrinsic bases of etiology. Those who had symptoms since birth were excluded.

Table 3 shows relation of duration of symptoms and clinical disease entity. It is evident that maximum number of patients had symptoms for 1 to 5 years. While only 6 had duration of symptoms less than one year.

TABLE 3 : Showing the duration of symptoms of various diseases.

Duration of symptoms (years)	No.of cases	Rhinitis	Asthma	Mixed	Urticaria
Group I ∠ 1	6	2	2	1	1
Group II 1 - 5	48	16	9	13	10
Group III 7 5	30	9	10	8	3
TOTAL	84	27	21	22	14

Table 4 shows agewise incidence of various diseases. Out of 27 cases of rhinitis in 7 cases symptoms occurred in second decade of life likewise in 11 patients in third. In 7 in 4th decade, and in one each in fifth and 7th decade of life. Same thing happened with asthma with maximum cases (15) occurred in 21-40 years age group while 2 occurring in 2nd decade, 4 in 5th and 2 cases in 6th decade. Mixed cases were also more in 3rd and 4th

decade. On the other hand urticaria cases were more in the first decade (5) and second decade (4).

TABLE 4 : Showing the agewise incidence of various allergic diseases.

Age groups (years)	Allergic rhinitis	Allergic asthma	Mixed	Urticaria
0 - 10	7	-	-	5
11 - 20	7	2	6	4
21 - 30	11	7	5	1
31 - 40	7	8	5	3
41 - 50	1	2	5	1
51 - 60	-	2	1	-
61 - 70	1	-	-	-
TOTAL	27	21	22	14

Table 5 shows the incidence of cases in relation to sex. Out of 27 cases of rhinitis, 15(55.6%) cases were males and 12(44.4%) were females. Asthma and asthma mixed with rhinitis were more in males, 62% and 63.6% respectively while urticaria was found in both sexes equally.

TABLE 5 : Showing the incidence of cases in relation to sex.

Sex (n)	Rhinitis	Asthma	Mixed	Urticaria
Males(49)	15(55.6)	13(62)	14(63.6)	7(50)
Females(35)	12(44.4)	8(38)	8(36.4)	7(50)
Total	27(100)	21(100)	22(100)	14(100)

Figures in parantheses are percentage.

TABLE 6 : Showing the period of maximum severity of various allergic diseases.

Period of year	Rhinitis	Asthma	Mixed	Urticaria
June-July	2	10	9	-
Aug.-Sept.	8	-	-	-
Oct.-Nov.	4	4	5	2
Dec.-Jan.	9	5	4	6
Feb.-March	4	2	3	-
April-May	-	-	1	-
TOTAL	27	21	22	14

Table 6 shows the period of year during which patients had maximum severity of symptoms. Allergic rhinitis cases were more prevalent during winters, 17 cases out of 27 had maximum severity of their illness from October to early March and these months bear minimum temperature. While allergic rhinitis had this distribution, Asthma cases had both poles, 10 out of 21 cases had peak during June to July months whereas 11 cases had their severity of symptoms from Oct. to March. Out of 14 urticaria cases taken, 6 had no peak of symptoms. They, infact had allergy to various food, clinically presenting as itchy rashes while 6 had clear peak during December and January months. Patients having symptoms of both Asthma and rhinitis had their peak during both the seasons.

Table 7 and 8 show symptomatology of allergic rhinitis and allergic asthma.

The most outstanding feature in allergic

rhinitis was occurrence of sneezing while rhinorrhoea was second common symptom. A large number of cases had systemic symptoms in the form of weakness, anorexia, mental depression, irritability and malaise, 2 patients had complaints of fever along with eye symptoms. Both severity and number of symptoms were more in female patients and 4 female patients gave history of anxiety reaction.

TABLE 7 : Showing the symptoms of allergic rhinitis.

Symptoms	Male		Female	
	No.	%	No.	%
1. Sneezing	12	44.50	12	44.50
2. Rhinorrhoea	10	37.00	9	33.40
3. Nasal congestion	4	14.80	10	14.80
4. Nasal pruritis	2	7.40	6	22.30
5. Eye symptoms	4	14.80	2	7.40
6. Systemic symptoms	7	25.90	9	33.40

TABLE 8 : Showing the symptoms of allergic asthma.

Sl. No.	Symptoms	Male		Female	
		No.	%	No.	%
1.	Cough	10	47.60	6	28.50
2.	Expectoration	4	19.00	-	-
3.	Wheezing	12	57.00	6	28.50
4.	Dyspnoea	13	61.90	8	38.00
5.	Systemic symptoms	5	23.80	2	9.50

In patients who were taken as allergic asthma patients, dyspnoea and wheezing remain the commonest symptoms and expectoration was the least common symptom, no female patient complaint of expectoration, the presence of systemic symptoms was less in asthma patients. Amongst the male patients 10 patients (47.6%) complaint of cough while the group of patients who were having symptoms of both syndromes, have symptoms as mentioned in table 7 and 8.

Table 9 shows the symptoms which were present in patients of urticaria.

TABLE 9 : Symptoms of urticaria.

Sl. No.	Symptoms	Number of cases	
		Male	Female
1.	Raised erythematous lesion	6	7
2.	Pruritis	5	5
3.	Potentiation of lesion by scartching	5	5
4.	Angioedema	2	-
5.	Hives, welts, mosquito bite like lesion	1	-
6.	Associated breathlessness and cough	2	-
7.	Associated symptoms of rhinitis	2	3
8.	Systemic symptoms	2	1

Most of the patients presented with raised maculopapular lesions associated with itching. Five male and five female patients had complaints of increase in the size of lesion and pruritis with scratching. Incidence of systemic symptoms associated with urticarial rash was too less.

Out of 27 cases labelled as allergic rhinitis cases when ENT check up was done it was found that 5 cases had sinusitis, 3 had deviated nasal septum with or without spur, 2 cases had tonsilitis or other throat infections. Similarly 4 patients were labelled as cases of infectious rhinitis. Patients having atrophic rhinitis and vasomotor rhinitis were excluded earlier.

Out of 27 patients of allergic rhinitis four patients had already underwent nasal and sinus operations (SMR, Antrostomy, Polypectomy).

Out of asthma patients, no patient was found to have restrictive disorder on spirometry. X-ray chest of two patients showed miliary shadow like appearance probably due to allergic alveolitis, another two patients had tubercular infiltration. Out of total 84 patients, 38 patients had peripheral blood eosinophilia of more than 4%. 24 patients had more than 10 percent count. Stool examination for ova and cyst were positive in 11 cases.

SKIN PRICK TEST (SPT)

After proper assessment the study group was subjected to skin prick test using allergen extracts supplied by E. Merck (I) Ltd.. Patients had stopped all medication at least five days prior to the test. If any deterioration was anticipated they were allowed to take bronchodilators. They were not kept fasting prior to test. The most of the tests were carried out in 2

sittings and 19 tests were carried out in one sitting.

Out of 84 patients, after releiving them of their anxiety and apprehension, only 8 patients had minor reactions in the form of palpitation, vertigo and nausea. 4 patients complained of itching at the injection site.

One patient had severe anaphylaxis after injecting histamine and he had to be managed vigorously. All the eight patients who had minor reactions did not require any treatment.

Out of 84 patients subjected to SPT, 41 came out to be positive. 29 patients had positive results with one or another dust components, 8 were sensitive with pollens and 2 patients each were sensitive to fungi and food.

TABLE 10 : Indicating the distribution of positive cases.

Allergen extracts	Number of cases.		
	Male	Female	Total
Dust components	13	16	29
Pollens	5	3	8
Fungi	1	1	2
Food	-	2	2
Others	-	-	-

Dust and its components have the maximum score of positive results (70.7%), while pollens scored(19.5%) fungi and food components shared approximately 5% each.

TABLE 11 : Showing the distribution of cases positive to dust components.

Dust component	Number of cases		
	Male	Female	Total
House dust	6	11	17
Paper dust	3	3	6
Cotton dust	1	1	2
Hay dust	1	2	3
D. Farinae	4	3	7
D. Pteronyssinus	-	-	-
TOTAL	15	20	35

Table 11 shows the distribution of cases positive to dust components. There appear discrepancy between results shown in table 11 and total number of sensitive cases. This is due to 6 patients who came out to be positive with more than one component. Two patients showed positive reaction with two components viz paper dust and cotton dust. Another two patients came out to be sensitive to house dust and dust mite (DF). Two patients were positive with paper dust and house dust.

TABLE 12 : Showing the number of cases sensitive to more than one component.

	Components	Number of cases		
		Male	Female	Total
I	Paper + cotton dust	1	1	2
II	Paper + House dust	-	2	2
III	House + dust mite(DF)	1	1	2

Out of seven patients who were positive to dust mite allergen, five patients had pure sensitivity against dust mite (D. farinae).

Two out of these five were medical students who had onset of their symptoms 2 years and four years back respectively. Since they have come to Jhansi and both of them had peak severity during rains and both have presented with rhinitis.

On other student had rhinitis with asthma and had increase in the severity of symptoms during winter season.

Two middle aged female patients also had reaction against dust mite allergen. Both of them were housewives.

Distribution of patients sensitive to dust mite is shown in table 13. Table 14 shows the distribution of cases positive to house dust.

Four other patients who were sensitive to house dust allergen had also sensitivity to other allergen extracts.

HD + DF = 2 cases ((DF = D. Farinae)
HD + PD = 2 cases (HD = House dust &
PD = Paper dust)

Two patients were sensitive to paper dust purely. Both of whom were office workers and had clinical syndrome of asthma plus rhinitis. Four other patients who were sensitive of one more allergen along with paper dust have included earlier.

Out of two patients who came out sensitive to hay dust , one had rhinitis with peak severity during

TABLE 13 : Showing the distribution of patients sensitive to dust mite.

Sl. No.	Age (years)/ sex	Occupation	Period of peak of symptoms	Change in		Clinical syndrome	Duration of disease (years)	Reaction
				occup-ation	Resi-dence			
1.	20/M	Student	Sept-Dec.	+	+	AR	2	DF
2.	50/F	Housewife	Aug.-Nov.	-	-	Asthma	10	DF
3.	18/M	Student	Nov.-Dec.	-	-	Asthma+AR	3	DF
4.	30/F	Housewife	July-Oct.	-	+	Asthma+AR	2	DF
5.	24/M	Student	Nov.-Jan.	+	+	AR	4	DF
6.	31/M	Outdoor worker	July-Aug.	-	-	Asthma	6	DF+HD
7.	16/F	Housewife	July-Sept.	-	-	AR	3	DF/HD

(AR = Allergic rhinitis, DF = Dust mite allergen, HD = House dust).

TABLE 14 : Showing the distribution of patients sensitive to house dust.

Sl. No.	Age (years)/ sex	Occupation	Period of peak of symptoms	Change in		Clinical syndrome	Duration of disease (years)	Reaction
				Occup-ation	Resi-dence			
1.	35/F	Housewife	April-June	-	-	Asthma	4	HD
2.	14/M	Student	June-July	-	-	Asthma+AR	2	HD
3.	22/M	Student	June-July	+	+	Asthma+AR	2	HD
4.	32/M	Clerk	March-Sept.	-	+	Asthma	6	HD
5.	20/M	Student	March-June	-	-	AR	4	HD
6.	25/M	Teacher	March-June	-	-	Asthma+AR	3	HD
7.	28/F	Housewife	-	+	-	Rhinitis	8	HD
8.	26/F	Housewife	-	-	-	Rhinitis	4	HD
9.	32/F	Housewife	May-Aug.	-	-	Rhinitis	5	HD
10.	14/F	Student	March-June	+	-	Rhinitis	4	HD
11.	14/F	Student	Feb.-July	+	-	Rhinitis	2	HD
12.	20/F	Student	-	-	-	Urticaria	2	HD
13.	40/F	Housewife	July/Aug.	-	-	Asthma+AR	6	HD

June to September. Other patient had urticaria occurring during late summers and early rains.

Two patients who were positive to cotton dust also had sensitivity to paper dust. One of them clinically had asthma and other one had allergic rhinitis.

Table 15 shows the characteristics of patients sensitive to various pollen extracts. The severity of symptoms occur during the pollenation season. Peak of symptoms for triticum sativum was observed during January and February. While that for Holoptelea integrifolia was seen during Jan.-March months. Patients showing sensitivity to parthenium hysterophorous had their peak of symptoms during the period of October to February.

The duration of illness (seasons during which patients were sensitive) was also more. Three patients were having symptoms for 8 to 10 seasons. Average duration of illness was 6.25 years.

Both the patients who were sensitive to fungus aspergillus flavus were having symptoms of asthma. One male patient had peak of symptoms during January to March while other patients had no definite peak.

Both the patients who were sensitive to food allergens, presented with urticarial rashes along with diarrhoea and vomitings. One patient had symptoms for two years and other non-vegetarian patient had symptoms for 10 years, and on exposure that is ingestion of particular food article, they had onset of symptoms.

TABLE 15 : Showing the characteristics of patients sensitive to various pollen extract.

Sl. No.	Age (years)/ sex	Occupation	Period of peak of symptoms	Change in		Clinical syndrome	Duration of disease (years)	Positive test
				Occup-ation	Resi-dence			
1.	14/F	Household work	Jan.-Feb.	-	-	Rhinitis	3	Tritium sativum
2.	35/F	Housewife	Oct.-Feb.	-	-	Rhinitis	10	Pennisetum typhoides
3.	18/M	Carpenter	Jan.-April	-	+	Rhinitis+ Asthma	10	Holoptelea Integrifolia
4.	25/M	Farmer	Jan.-Feb.	-	-	Urticaria	5	Triticum sativum
5.	32/M	Plumber	Jan.-March	-	-	Rhinitis	6	Holoptelea Integrifolia
6.	20/M	Student	Oct.-Dec.	+	+	Urticaria	4	Parthenium Hysterophorous
7.	50/F	Housewife	Jan.-April	-	-	Asthma	10	Holoptelea Integrifolia
8.	44/M	Farmer	Oct.-Feb.	-	-	Urticaria	2	Parthenium Hysterophorous

IMMUNOTHERAPY

Eighty four patients who were subjected to SPT, 41 out of them were sensitive to one or the other allergen. All of them were advised to undergo immunotherapy. However, 23 could be subjected to hyposensitization. 6 out of these 23 only received treatment, no maintenance therapy could be given.

Four patients interrupted the treatment hyper-sensitization and had to be given that strength of treatment from initial dose.

The scheme of increase in dose (concentration of allergen extract is shown in annexure - III).

Table 16 shows the distribution of patients who underwent hyposensitization. Person sensitive to more than one allergen are counted separately for each allergen.

Patients who were positive with food stuff were advised only avoidance. They were not put on immunotherapy. Distribution of cases sensitive to particular allergen is as follows :

Dust component	Pollen	Fungi	Total
14	7	2	23

However, 3 patients in the dust component category were positive to more than one allergen.

TABLE 16 : Distribution of patients underwent hypo-sensitization.

Name of Allergens	Male patients		Female patients		Total
	Sensitive to purely	Sensitivity in combination	Sensitive to purely	Sensitivity in combination	
A. DUST					
House dust	3	1	1	1	
Cotton dust	-	1	-	-	
Paper dust	2	1	-	1	17
Hay dust	-	-	-	-	
Dust mite	3	1	2	-	
B. POLLEN					
Triticum sativum	1	-	1	-	
Pennisetum typhoides	-	-	1	-	7
Holoptelea Integrifolia	3	-	-	-	
Parthenium Hysterophorous	1	-	-	-	
C. FUNGUS					
Aspergillus flavus	1	-	1	-	2
D. FOOD ALLERGENS					
Lemon and tomato	-	-	-	-	
Chicken	-	-	-	-	

DISCUSSION

D I S C U S S I O N

Allergic disorders put an ever existing challenge, if their prevalence, impact on the life and occupation of patient, their long exhausting course and continued need of drugs are considered. Patients who have seasonal allergic rhinitis or asthma, name the season as that of discomfort and abstinence from work. Condition becomes more miserable when drug treatment does not suffice or patient finds it difficult to live on drugs.

The determination that a clinical syndrome may have an allergic etiology is important, because specific prophylactic and therapeutic interventions can be used once an allergic cause has been identified. For curative treatment is is essential that allergens responsible for the symptoms by accurately identified. There are different ways to arrive at a diagnosis. Case history remains extremely important in all allergological investigations. Skin test procedures can be employed to identify responsible allergens. The size of skin reaction, the dose of allergen required to produce a given skin reaction size, and number of positive skin tests, all provide a clue regarding the etiology and severity of disease.

Clinically, immediate hypersensitivity skin test has been demonstrated to have predictive diagnostic value. Subjects with a history of an allergic syndrome

occurring on exposure to allergen and with skin test reactivity at low doses of that allergen are at a very high risk of experiencing a recurrence of the allergic syndrome when they are re-exposed to that allergen (Norman, 1973 and Hunt et al, 1978). The degree and number of positive skin tests to a battery of allergens have also been demonstrated to be positively associated with the reported prevalence of allergic diseases in the population (Burrows et al, 1976 and Haahtele et al, 1980). Furthermore, asymptomatic subjects, who are skin test positive, are at a higher risk of developing an allergic syndrome (Chambers, 1958 and Hagy, 1976).

Allergy skin testing is, therefore, a useful objective clinical method for evaluating the prevalence of immediate hypersensitivity to selected allergens. In addition, allergy skin tests are ideally suited for population surveys because multiple tests can be performed within a short period of time.

Age had been an important indicator of reactivity in all multivariate analyses. Hendrick et al (1975) and Barbee (1981) have reported that there is a decrease in skin reactivity with advancing age. Peak skin test reactivity had been seen in age group of 20-40 years. Diminished and organ responsiveness in infants and elderly individuals to inflammatory mediators appears to be one contributory mechanism (Van Asperen et al, 1984 and

Gilchrest et al, 1982). There is an age associated loss of vascular bed(50% reduction of mast cells and 35% reduction of venular cross section) also there is a decrease in histamine release with age. A decrease in skin response to mast cells degranulating agents has been reported in infants (Menardo et al, 1985). According to other workers, differences in allergen exposure with age, immunologic responsivity, or tissue differences are responsible for the age related differences in SPT results (Gergen et al, 1986). Results of our study do concide with these observations. The IgE increase during these years of age and proliferative capacity of clonable T and B cells during 25-35 years which decline in later years of life (Kay, 1979) may provide a further explanation to this age related change.

Many studies have been conducted to find out the relation of sex and SPT reactivity. In our study no clear cut trend could be made out. Out of 8 patients who showed reactivity against pollen allergens, 5 were males and three were females, while in those who showed sensitivity against dust components, 5 were males and 8 were females. Amongst patients showing sensitivity to dust mite allergen, four were males and three were females.

Male predominance in allergen skin test reactivity could be expected due to higher levels of IgE in men as compared to women (Freidnoff et al, 1984).

Lindblad et al (1961) and Haahtele et al (1979) have also reported more reactivity among males. Pollen

reactivity and dust mite reactivity in present study showed similar trend.

In present study out of 41 patients who showed reactivity against one or more allergen, 26 were resident of urban area while 15 belonged to rural locality. Residency in urban area was an indicator for increased reactivity in all multivariate analyses (Peter Gergen, 1986). Linna (1974) also found in his study that skin reactivity was more in urban dwellers. Smith et al(1982) have reported the same or lower incidence of reactivity in rural population.

The reason for this could be urban clustering of families with positive allergic history or cultural differences in the urban and rural groups. It may be related to pollutants in the urban environment. This is also evident in increasing incidence of allergic diseases with rapid urbanization.

Other variables that may affect SPT reactivity are poverty, education and income. Barbee et al (1976) found increasing reactivity with increasing income. Linna (1974) found more reactivity among educated group.

In present study these variables have affected the results in similar way.

In present study all the tests had been conducted in the morning and before noon. It is often questioned that does circadian variation affect SPT result. Pakit Vichyanond et al (1989) have shown that there is no

significant morning, evening variation in SPT results. Earlier Reinberg et al (1965) and Lee et al (1977) have put similar opinion after their studies. So, it does not affect the result, whether, the SPT is performed in the morning or evening.

The inclusion of positive control (Histamine) in SPT is recommended for optimal evaluation of allergen hyper sensitivity (Nelson, 1983 and Malling, 1984). Some investigators advocate semiquantitative grading of skin test reactions to allergens based on a percent size of a positive control reaction (Aas, 1980). We in present study used histamine as positive control but Casale et al (1984) propose to us codeine, which triggers mast cell release via specific cellular receptor while histamine is an end organ mediator.

It has been demonstrated that histamine reactivity is lower in infants and in old persons. Skassa Brociek (1985) has proposed that reactivity to histamine increases uptil adulthood, decreases after 50 years and there is plateau after 60 years. As size of SPT reaction to histamine varies with age, therefore, the interpretation of skin tests should not only take into account the wheel size but rather a ratio between histamine induced and allergen induced wheals.

Wheal size produced with histamine in present study was 6 mm to 10 mm. Four patients did not show reaction to histamine, two of them were more than 50 years

of age while one patient was of 44 years of age. The remaining one was 26 years old female. Perhaps they did not comply to stopping all medication(including antihistaminics) prior to test or the age criteria proposed earlier could be the possible cause of poor reactivity.

Richard Horsinger (1972) pointed towards correlation of allergic asthma and peripheral eosinophil count. Tandon and Saha (1987) found that in their study only 55% of SPT positive patients had raised eosinophil count. In present study patients having high eosinophil count were 18 out of 41 positive results.

Despite the development of various in vitro methods, skin testing with potent allergen preparation and positive and negative control substances, remains the most revealing procedure in diagnosing specific allergic factors associated with allergic diseases. When merits of SPT and RAST (Radio-allergosorbent test) are compared. It has been found that :

1. Both tests detect IgE antibodies accurately and reproducibly.
2. Both the tests reveal information of a semiquantitative nature, but SPT is more sensitive.
3. Results of both tests correlate equally well with allergic symptoms.
4. Both tests can be used as grounds for instituting immunotherapy.

5. Skin tests appears to be superior in diagnosis of life threatening anaphylactic state in which maximum sensitivity is important.

6. The results of SPT are more immediately available (within ½ an hour) in comparison to 2-3 days required for RAST results. However, presence of dermatographia, widespread skin diseases and patients apprehension of pricks may be regarded as states of non-applicability of SPT.

Rosario scolozzi et al (1987) compared SPT with multiple chemiluminescent assay (MAST-CLA) and they propose that no technique is as sensitive as skin tests for allergen specific diagnosis of inhalant allergic disease.

Finnerty et al (1989) have also weighted SPT and MAST and they found both the procedures equally effective.

Prick et al (1989) in their study on asthmatic children allergic to inhalants, compared SPT with other in vitro techniques and they also found SPT more effective.

SPT can act as predictive indicator, Chambers (1958) and Hajy et al (1976) have proposed that asymptomatic subjects, who are SPT positive to certain allergen are at higher risk of developing an allergic syndrome.

Skin prick test has also been compared with direct provocation tests. Warner (1976) and Panli (1977) found strong correlation between SPT and bronchial

challenge test, but the latter test does not mimic a realistic exposure to house dust. In bronchial challenge test, results are assigned according to symptom - score, and positivity is ascertained on the bases of total score.

Clinical bronchial score :

Symptoms	Score
Cough	1
Breathlessness	2
Tightness	1
Wheezing	4

Raihi (1990)

This technique does not quantify the amount of material required to prove bronchial reaction.

Cockroft et al (1979) and Spector et al (1979) could not demonstrate any correlation between cutaneous and bronchial responsiveness.

Peter small (1989) studied the correlation between SPT and nasal provocation test. He concluded that properly performed SPT predicts nasal reactivity to the same allergen, that is nasal provocation adds least to the information yielded by SPT. Direct IgE measurement and SPT result correlation has also been studied. Bernard Berman et al (1986) could not find any statistically signifiant differences when they compared SPT results and direct IgE measurement in the light of clinical picture.

According to William Knicker (1989), more sensitive test (SPT) lend more opportunity for false

positive interpretations while less sensitive test (RAST) provide more chances of false negative interpretation.

COMPARISON OF SKIN TESTING WITH IN VITRO TECHNIQUES:

	Skin testing	In vitro techniques
Time	15 min + 4/6 hrs.	5 hours to 2-3 days
Specificity	Allergen dependent skin site dependent.	Allergen dependent IgE dependent.
Sensitivity	Varies(⩾0.01 IU/ml)	0.01 IU/ml.
Risk	Systemic reactions false positive.	False negative.

In this way excluding few short comings, SPT is a convenient and useful technique in the confirmation of allergic etiology of disease.

Using SPT, Lyndon mansfield et al (1988) put an idea of local miniscreen for detection of allergic disease which would provide an accurate referal. This miniscreen included SPT and IgE assay.

Rodriguer et al (1988) has documented hetrogenecity in skin tests results, when the tests were done by 4 different practices using the same panel of allergens. The difference in performing test, different in the criteria of reading result and difference in the standardization and concentration of allergen extracts lead to hetrogenecity in test results.

In our study we performed skin prick test using a lancet with free hand technique. Standreborg et al

(1987) compared this technique with, that, using a glass syringe attached to a micrometer, but they found no difference in results.

It is being questioned that does it make any difference if different area of human skin is taken(like forearm and back) for SPT. Voorhorst (1973) compared the two and reported that SPT results vary. Stendreborg et al (1987) also did a comparison. But both these studies could not find a common pattern for variation. In present study we prefered forearm to do SPT in order to avoid this discrepancy.

From time to time various studies have been conducted to assess the prevalence of various allergens. This exervise provides etiological precision along with guiding the approach of the management of allergic diseases prevalent in a particular locality. In general the group of allergen which are tested include dusts and dust mites, pollens of various plants and trees, molds, food allergens and industrial products. Physical agents and industrial products are tested for their allergenic implications by patch test.

Like present study many workers have studied the prevalence of various allergens along with associated characteristics. In present study out of 84 patients tested of their allergic disorders, 41 showed positive SPT. Out of these 41, 29 patients have shown positive reaction with dust components and dust mite allergenic extracts.

8 patients have shown positive reaction with pollens while 2 each have shown positive reaction with fungi and food component.

Table 10 shows the distribution of reactivity of 41 patients. Maximum sensitivity has been found against dust and dust mite. Persons who were positive to house dust alone had the peak severity of their symptoms in summers. The hot and dusty climate of Bundelkhand region during summers well complies with the statement.

Maunsell et al (1968) conducted study to evaluate allergic etiology of bronchial asthma. In most of their study group patients, dust and dust mite (Dermatophagoides) were triggering factors of asthma.

Tandon and Saha (1987) analysed the house dust from the houses of 20 bronchial asthma patients suspected to have sensitivity against house dust. They found almost similar levels of infestation by Pteronyssinus and Farinae mites in homes of asthmatics and control, meaning thereby that it is the reactivity of individual to particular allergen which results into clinical syndrome. In this way, only measurement of levels of mite in house dust cannot provide solid grounds for making diagnosis. Dixit and Mehta (1973) had similar opinion.

Tripathi and Parikh (1983) after studying allergens in Bombay had found that maximum number of positive patients were sensitive to one of the component of dust, and D. farinae plays an important role in house dust allergy.

For the growth and persistence of dust mites low temperatures are required, but Tandon and Saha (1987) have conducted their study in Calcutta and Tripathi and Parikh (1983) did their study in Bombay. At both the places, temperature is more than 30°C during most of the months. Second requisite is humidity or more than 50%. In present study five patients were positive to dust mite alone. In all of them peak severity of their symptoms were during November and December.

Two patients had sensitivity against dust mite allergen along with one more allergen. Two possibilities can be put on the basis of above results. Either house dust of these patients or the dust around their residences is infested with dust mites or the growth of dust mites occurs during winters or rains when the conditions are suitable for their growth. Dust samples should be investigated for dust mite and it has been decided to investigate dust samples from appropriate places in and around the residences of these patients.

In international workshop report, Germany, 1987 HR Ranganath from Bangalore had reported a high prevalence of mite allergy among subjects with asthma and a high number of mite in house dust of these patients.

Sometimes patients relate triggering of their symptoms and exposure to house dust, but who are actually sensitive to some other allergen, or their symptoms do not have an allergic base. Murray (1983) found discre-

pancy between number of patients giving history of house dust sensitivity and number of patients coming out positive on SPT.

Dust components sensitive asthmatic patients sometimes develop pollen sensitive allergic rhinitis. Smith (1978) explained this on the bases that asthma and rhinitis are related to each other. However, study of Masanau Shibasaki (1990), proposes that these two are independent of each other and allergic rhinitis developing in patients of bronchial asthma should be looked upon as separate entity. According to Ranson (1989), mite antigen level of 2 ug/g is associated with risk of allergic sensitization, but according to Wood et al (1987) a level of 1 ug/g is associated with significant risk.

Many studies have been conducted to find out the prevalence of various allergen in the environment of a particular city. Lakhan Pal and Nau (1960) conducted their study in Almora, Singh et al (1981) in Amritsar while Tripathi et al (1982) conducted their study in Bombay, Shivpuri (1980) and Singh Babu (1980) have conducted similar studies in Delhi.

John Santilli (1988) did his study using SPT with mold extracts and he obtained many positive results. He proposed that panel of allergens to which patients are subjected while performing SPT should also contain mold extract allergens.

When observant patients can provide fairly exact dates of onset and offset of seasonal symptoms, correlation with allergen known to occur in that pollenating season in patient's environment, can provide important diagnostic information.

RATIONALE OF IMMUNOTHERAPY

When incremental doses of a specific allergen extract, known to produce allergic symptoms in an individual are administered over a certain period of time. Patients tolerance to that allergen increases on natural exposure and patient's symptoms are significantly diminished or ameliorated. Various studies support the efficacy of immunotherapy. Horman (1974), Van Metre et al (1980) Normal and Lichtenstein (1978). Studies of these workers support the efficacy of immunotherapy. Some other studies provide an objective measurement of improvement following immunotherapy. Aas (1971) has shown decreased bronchial sensitivity to dust extract in persons who had immunotherapy against dust allergen. Warner et al (1978) conducted a double blind study and reported that 50% of patients receiving immunotherapy had resolution of late phase of bronchial reactivity on bronchial challenge.

Bousquet et al (1985) demonstrated that skin prick test reactivity also decreased in patients who received effective immunotherapy.

Along with clinical improvement, efficacy of

immunotherapy is judged by immunological and mediator response.

Both WHO and FDA have attempted to standardize immunotherapeutic (in context of allergic diseases) preparations so that they can be safely used and results of two different studies can be compared.

Immunotherapy is generally recommended in cases where avoidance is not feasible and in cases where drug therapy becomes palliative. Immunotherapy is allergen specific and dose dependent. High dose therapy is superior to low dose therapy. Patients undergoing immunotherapy subsequently develop antibodies (Blocking antibodies) that are capable of blocking passive transfer reaction.

Allergic extracts which are deployed in hyposensitization are either aqueous extracts, depot extracts or modified extracts.

Both local and systemic reactions may occur with immunotherapy. A recrudescence of symptoms may occur on discontinuation of therapy (Creticos et al, 1987). Though hyposensitization is quite safe but severe life threatening anaphylaxis may be observed but very rarely and this may be followed more rarely by death (Schaeffer and Sisk, 1984). Excluding the unexplained cause, error or dose selection could be possible cause of this. Patient should be kept under supervision for about 2 hours after therapy.

Reactions occurring early in the course of therapy are because immunotherapy stimulates IgE production but no IgG protection. According to one CSM report (1986), 30% patients may experience minor reactions. 6 of our patients complaint of nausea, dizziness but drop in blood pressure was recorded in only one patient.

In the employment of immunotherapy following methods have been proposed :

A. Preseasonal method.

B. Co-seasonal method.

C. Perennial method.

Preseasonal method is employed for seasonal allergens especially pollens, the treatment is started in such a way that maintenance dose is reached before the start of season.

In co-seasonal method, injections are given throughout the season in which patients have complaints.

In perennial method, after a top dose in the preseasonal method is attained, It becomes possible to continue treatment by administering a dose just below that of top tolerable dose every 3 or 4 weeks, top well tolerated dose is continued at 2 to 3 weeks interval throughout the year.

Dose schedule used in present study is given in annexure - III.

The immunological bases of improvement provided by immunotherapy are :

1. There occurs a rise in serum IgG antibodies.
2. There occurs a blunting of the usual seasonal rise in IgE antibodies followed by a slow decline in the peak level of a specific IgE antibodies during immunotherapy.
3. There is elevation of blocking IgA and IgG antibodies in nasal secretions.
4. There is a decrease in basophil histamine releasibility when cells are incubated with allergen.
5. There is a reduction in vitro lymphocyte responsiveness to specific allergens.
6. There is a generation of specific suppressor T cells.
7. There is blunting of the late skin and brochial responses.

IgG antibodies which are produced following immunotherapy have high affinity for allergens but form nonspecific immune complexes that do not fix complement, and there occurs no immune complex mediated diseases.

A favourable clinical response to immunotherapy is found in the ratio IgG/IgE, that is protective immunologic responses mediated by IgG antibodies balancing out the allergic immunologic responses mediated by IgE antibodies. Studies have suggested that immunotherapy

that does not induce IgG antibody response, is not associated with measurable clinical response. Sometimes when immunotherapy is done with unstandardized allergen extract with low potency, results are not satisfactory.

Failure of immunotherapy may occur due to improper assessment of culprit allergen which may be due to use of conservative cut off point to define SPT positivity.

If the patient is sensitive to allergen other than used in certain study. Test may not detect the causative allergen.

S U M M A R Y

S U M M A R Y

A precise and objective approach appears reasonable when the management of allergic disorders is considered. As a routine, these disorders are treated on general lines with the result the patients continue to suffer.

In order to evaluate the role of intercutaneous skin prick test and efficacy of immunotherapy in the management of allergic diseases (Allergic bronchial asthma, allergic rhinitis, urticaria), present study was conducted in eighty four patients clinically suspected to suffer from one or the another allergic disease. The study was aimed to confirm the allergic etiology of disease by subjecting patients to skin prick test (SPT) using 84 allergenic extracts. Commoner allergens present in the environment of Bundelkhand region were outlined on the bases of results of SPT.

Patients who showed positive reactions were then put on immunotherapy, protocol of which is based on immunizing a patient with a series of injections twice a week or thrice a week with gradually increasing doses starting so low as to obviate any risk of untoward allergic reaction. As controlled clinical studies of allergen immunotherapy demonstrate that results obtained after immunotherapy are specific and relapse may occur on discontinuation of maintenance immunotherapy, Those persons who underwent treatment were advised to undergo maintenance therapy.

Cases in the present study have been selected on the basis of clinical history and exclusion of other possible etiologies (Primary asthma, tuberculosis, TPE etc.) of their illness by appropriate investigations. It had been a multivariate approach i.e. patients of all ages, both sexes and of various socio-economic strata were included. They had other variables in their characteristics like occupation, habitat and severity of disease in a particular season. Most of them had a long course of their illness.

After proper assessment, on putting to SPT, excluding eight patients who complainted of minor reactions, Rest all the patients could tolerate without any problem. Out of eighty four patients, fourty one (49%) cases came out to be sensitive to one or more than one allergen. Out of positive cases 70.7% were sensitive to one of the dust components or to a combination. 19.5% were sensitive to pollens. 5% were sensitive to one of the fungi while another 5% were sensitive to food components.

Other trends which could be made out were that peak skin reactivity is present in the third decade and fourth decade. Sex of the patients does not make a direct impact on results. Incidence of diseases was more in urban population. It is also being observed that Histamine reactivity also changes from person to person and at different age. Another fact was that in every atopic patient raised peripheral eosinophil count was not found.

Persons who were undergoing immunotherapy were then again subjected to SPT. 23 patients out of positive cases could be subjected to immunotherapy and after completion of treatment set all of them observed subjective improvement of their symptoms, their skin test reactivity also decreased after treatment, when they were put on SPT again, Thus providing an objective evidence of improvement.

CONCLUSION

CONCLUSION

Following conclusions have been drawn from the study.

1. All patients supposed to suffer from allergic disorders should be subjected to SPT as this segregation helps to treat SPT positive persons more precisely and accurately.

2. Persons who did not show positive reaction to a battery of 84 allergens might have sensitivity against some other allergens which are not tested for.

3. Majority of patients suffer allergic disorders in their 2nd or 3rd decade of life. Histamine reactivity also changes with age. Sex does not clearly affect the incidence.

4. Allergic diseases are more common in urban population. Recent change in persons environment due to change in occupation or residence exposes the persons to new battery of allergens.

5. No circadian variation is seen in the results of SPT.

6. SPT is the most revealing procedure in diagnosing specific allergic factors. It is economical, safer, less time consuming, and the results obtained are as accurate as being obtained by most modern or most sophisticated techniques.

7. Commonest allergens were dust components with maximum reactivity against house dust (17), dust mite (7), paper dust (6) and others (5).

8. Amongst pollens, commoner were Holoptelea intergifolia (3), Triticum sativum (2) and Others(2).

9. Growth of dust mite requires low temperature and more humidity. In Bundelkhand region either these appropriate conditions are present in winters which favour their growth or the person who showed positive reaction to dust mite, did so due to cross reactivity with some other dust component.

10. Immunotherapy is quite significant procedure in the management of allergic disorders. Preseasonal, perenial or co-seasonal method of its employment and proper maintenance therapy should be carried out in every SPT positive patients.

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MASTER CHART

MASTER CHART

Sl. No.	Name of patient	Age (years)/ Sex	Symptoms	Occupation	Urban/ rural	Veg./ non-veg.
1	2	3	4	5	6	7
1.	Dilip Mason	20/M	Rhinitis	Medico	U	NV
2.	Shashi	35/F	Asthma	House wife	U	V
3.	Sanjay	27/M	Asthma	Advocate	U	NV
4.	Karan Singh	17/M	Rhinitis	Student	R	V
5.	M. Kumar	14/M	Rhinitis+ Asthma	Student	R	V
6.	B. Deen	40/M	Rhinitis	Business	R	NV
7.	Kalpana	21/F	Rhinitis+ Asthma	Student	U	V
8.	Patram	27/M	Rhinitis+ Asthma	Clerk	U	NV
9.	Prof.D.N.M.	46/M	Rhinitis	Medico	U	V
10.	HC Jain	66/M	Rhinitis	Shopkeeper	U	V
11.	SD Srivastava	32/M	Asthma	Clerk	U	NV
12.	BP Singh	35/M	Rhinitis+ Asthma	Bank Employee	U	NV
13.	Pratibha	180F	Rhinitis	Student	U	NV
14.	VK Philip	32/M	Asthma	Surveyer	R	NV
15.	Pushpa	50/F	Asthma	House wife	U	V
16.	Geeta	35/F	Asthma+ Rhinitis	House wife	U	V
17.	G. Lal	32/M	-do-	Watchman	R	V
18.	Shabir Ahd	34/M	Asthma	Rty Employee	U	NV
19.	Rajeev	28/M	Rhinitis	Medico	U	V
20.	Dharmesh	21/M	Asthma + Rhinitis	Student	U	V
21.	Rajii	22/M	-do-	Medico	U	NV
22.	RK Ashok	28/M	Asthma	Medico	U	V
23.	Ahluwalia	51/M	Asthma	Bank employee	U	NV
24.	Jaidevi	14/F	Rhinitis	House girl	R	V
25.	Upendra	18/M	Asthma + Rhinitis	Student	U	NV
26.	Omwati	26/F	Rhinitis	House wife	U	V
27.	Vinod	32/M	Asthma	Clerk	U	NV
28.	Munni Devi	30/F	Asthma + Rhinitis	House wife	U	V

1	2	3	4	5	6	7
29.	Sunil	20/M	Rhinitis	Student	U	NV
30.	Jagat	30/M	Rhinitis	Farmer	R	NV
31.	Manju	8/F	Urticaria	Student	R	V
32.	Nathuram	32/M	Asthma	Watchman	U	NV
33.	PC Gupta	50/M	Asthma	Retired GS	U	V
34.	Babulal	31/M	Asthma	MPSEB	R	V
35.	Mrs. Gautam	26/F	Asthma	Teacher	U	NV
36.	Sunil Kumar	20/M	Asthma + Rhinitis	Student	U	NV
37.	Ramdevi	26/F	Asthma	House wife	U	V
38.	Shakuntala	35/F	Rhinitis	House wife	R	V
39.	Nitin Sirohi	16/M	Asthma	Student	U	NV
40.	Kailash	30/M	Asthma	Business	U	V
41.	Jai Prakash	25/M	Asthma + Rhinitis	Teacher	R	V
42.	Sameer Gupta	9/M	Urticaria	Student	U	V
43.	Satish	35/M	Rhinitis	Govt. Serv.	R	V
44.	Babita	28/F	Asthma	House wife	U	V
45.	Anoop	12/M	Asthma + Rhinitis	Student	U	V
46.	Jaidevi	15/F	Rhinitis + Asthma	Student	R	NV
47.	Deepak	180M	Asthma + Rhinitis	Carpenter	U	NV
48.	Gambhir	25/M	Food(N)	Farmer	R	NV
49.	Ranjana	28/F	Rhinitis	House wife	R	V
50.	PK Jain	40/M	Asthma + Rhinitis	Medico	U	V
51.	Chanda	26/F	Rhinitis	House wife	R	V
52.	Sirajuddin	32/M	Rhinitis	Plumber	U	NV
53.	Shairabano	35/F	Food(U)	House wife	U	NV
54.	Naresh	24/M	Rhinitis	Medico	U	V
55.	Indira	26/F	Rhinitis	House wife	U	NV
56.	PP Singh	28/M	Asthma	Shop keeper	U	NV
57.	Amrit Singh	20/M	Urticaria	Student	U	NV
58.	Shakuntala	44/F	Asthma + Rhinitis	House wife	R	V

1	2	3	4	5	6	7
59.	PN Misuriya	42/M	Asthma	Govt.Execu.	U	V
60.	Jyoti	32/F	Rhinitis	Housewife	U	V
61.	Aneeta Devi	10/F	Urticaria	House girl	U	V
62.	Nafeesa	52/F	Asthma +	House wife	R	NV
63.	Shayama	32/F	Rhinitis	House wife	U	V
64.	RK Tewari	30/M	Rhinitis	Teacher	R	V
65.	Kalyani	14/F	Rhinitis	Student	U	V
66.	Uttam Chand	38/M	Rhinitis	Contractor	U	V
67.	Krishna	50/F	Asthma	House wife	R	V
68.	Seeta Devi	34/F	Asthma + Rhinitis	House wife	R	V
69.	Parwati	10/F	Urticaria	Student	R	V
70.	S. Narayan	40/M	Food (U)	Business	R	V
71.	Kanta	16/F	Rhinitis	House girl	U	NV
72.	Sant Ram	44/M	Asthma + Rhinitis	Clerk	U	NV
73.	Kaisher	10/M	Urticaria	Student	U	V
74.	Anneta	26/F	Rhinitis	House wife	U	NV
75.	Baldev	44/M	Urticaria	Farmer	R	NV
76.	Shanti	56/F	Asthma	House wife	R	V
77.	Abha	14/F	Rhinitis	Student	U	V
78.	YP Singh	44/M	Asthma + Rhinitis	Govt. Serv.	U	NV
79.	Sultana	20/F	Food (U)	House wife	R	NV
80.	Bhavna	20/F	Urticaria	Student	U	V
81.	Nathu	30/M	Rhinitis	Washerman	U	NV
82.	Ramwati	40/F	Asthma + Rhinitis	House wife	R	V
83.	Amita	18/F	Urticaria(F)	Student	U	V
84.	PC Gupta	40/M	Urticaria(F)	Business	U	V

U = Urban, R = Rural, V = Vegetarian
NV = Non-vegetarian

Sl. No.		Change in Occupation	Change in Residence	Duration of symptoms	Result	Mode of treatment
1	2	3	4	5	6	7
1.	S	+	+	2 years	DF	IT
2.	S	-	-	4 yesrs	HD	-
3.	S	-	-	5 months	-	-
4.	S	-	-	6 years	-	-
5.	S	-	-	2 years	HD	IT
6.	A	+	+	3 years	-	-
7.	S	-	-	7-8 months	-	-
8.	S	-	-	5 years	PD	IT
9.	S	-	-	5 years	-	-
10.	S	-	-	4 years	-	-
11.	S	-	-	2 years	-	-
12.	S	-	-	3 years	PD	IT
13.	S	+	-	5 years	-	-
14.	A	+	+	8 years	-	-
15.	S	-	-	10 years	DF	IT
16.	S	-	-	15 years	-	-
17.	A	-	-	10 years	-	-
18.	S	-	-	2 years	Aspergillus flavus	IT
19.	S	+	+	9 years	-	-
20.	S	-	-	10 years	-	-
21.	S	+	+	2 years	HD	-
22.	S	+	+	7 years	-	-
23.	S	-	-	7 years	-	-
24.	S	-	-	3 years	Tritium Sativum	IT
25.	S	-	-	3 years	DF	IT
26.	S	+	+	7 years	-	-
27.	S	-	+	6 years	HD	-
28.	S	+	-	2 years	DF	IT
29.	S	-	-	4 years	HD	IT
30.	A	-	-	3 years	-	-

1	2	3	4	5	6	7
31.	S	-	-	10 months	-	-
32.	A	+	+	5 years	-	-
33.	S	-	-	15 years	PD + CD	IT
34.	A	-	-	6 years	HD + DF	IT
35.	S	+	+	4 years	PD + HD	IT
36.	S	-	-	6 years	-	-
37.	S	-	-	6 years	Aspergillus flavus	IT
38.	S	-	-	10 years	Pennisetum Typhoides	IT
39.	A	-	-	10 years	-	-
40.	A	-	+	4 years	-	-
41.	A	-	-	3 years	HD	IT
42.	A	-	-	6 years	-	-
43.	A	+	+	2 years	-	-
44.	S	-	-	4 years	PD+HD	-
45.	A	-	-	1 year	-	-
46.	A	-	-	2½ years	-	-
47.	A	-	+	10 years	Holoptelea integrifolia	IT
48.	A	-	-	5 years	Triticum Sativum	IT
49.	S	+	-	8 years	HD	-
50.	S	-	-	10 years	-	-
51.	S	-	-	6 years	Hay dust	-
52.	S	x	x	6 years	Holoptelea integrifolia	IT
53.	S	-	-	5 years	-	-
54.	S	+	+	4 years	DF	IT
55.	S	-	-	4 years	HD	-
56.	A	-	+	2½ years	-	-
57.	A	+	+	4 years	Parthenium Hysterophorous	IT
58.	A	-	-	6 years	-	-
59.	S	-	-	4 months	-	-
60.	S	+	-	2 years	PD + CD	-

1	2	3	4	5	6	7
61.	S	-	-	4 years	Hay dust	-
62.	A	+	-	2 years	-	-
63.	A	-	-	5 years	HD	-
64.	A	+	-	6 years	-	-
65.	A	+	-	4 years	HD	IT
66.	A	-	-	2 months	-	-
67.	S	-	-	10 months	Holoptelea integrifolia	IT
68.	S	-	-	5 years	-	-
69.	S	+	-	2 years	Tomato, Lemon	Avoidance
70.	A	-	-	8 years	-	-
71.	S	-	-	3 years	HD + DF	-
72.	S	-	-	3 years	Hay dust	-
73.	A	-	-	1 year	-	-
74.	S	-	-	6 months	-	-
75.	A	-	-	2 years	Parthenium Hysterophorous	-
76.	S	-	-	10 years	-	-
77.	A	+	-	2 years	HD	-
78.	S	-	-	4 years	-	-
79.	S	-	-	10 years	Chicken	Avoidance
80.	S	-	-	2 years	HD	-
81.	A	+	-	5 years	-	-
82.	A	-	-	6 years	HD	-
83.	A	-	-	2 years	-	-
84.	A	-	-	2 years	-	-

A P P E N D I X

WORKING PROFORMA

DEPARTMENT OF MEDICINE, M.L.B. MEDICAL COLLEGE, JHANSI

TO STUDY ALLERGY DETECTION TEST

Ref. No. Dated:

Name of the Patient :

Age/Sex

Occupation/Nature of work :

Address :

Location of Residence :

In Town In country New / Old Damp / Near water

Recent changes in : Residence Kaccha/Pakka Specific out door environment

Recent changes in Occupation :

Complaints Duration

1.

2.

3.

4.

5.

Age at which symptoms first appeared:

Severity of symptoms : Severe

Moderate

Mild

Are Symptoms : Static

Getting better

Getting worse

Specific period or weather in which symptoms appear or increase in their severity.

Frequency of symptoms : Constant

Intermittent

Onset of symptoms : Immediate

Slowly some hour later

Any specific hour of day during which symptoms occur.

Animal contacts at Home or work :

Any food article cause symptoms :

Any drug causes symptoms :

Has any blood relation suffered from any of allergic disorder. Yes/No

If yes : Relation :

Condition :

Current Medication :

INVESTIGATIONS.

Blood : T.L.C. cells/cmm.

D.L.C. : P , L , E , B , M

E.S.R. : mm in first hour.

Blood sugar : mg%

Blood Urea : mg%

Others :

Urine : Albumin

Sugar

M/E

X-Ray Chest :

E.C.G. :

Lung function tests :

Result of test :

ANNEXURE - II

LIST OF DESENSOL SKIN TEST SOLUTIONS FOR PRICK TESTING

A. POLLEN

1. Chenopodium album
2. Amatanthus spinosus
3. Argemone mexicana
4. Xanthium strumarium
5. Cynodon dactylon
6. Cyperus rotundus
7. Ricinus communis
8. Holoptelea integrifolia
9. Typha angustata
10. Zea mays
11. Cocos nucifera
12. Prosopis juliflora
13. Putrajiva roxburghii
14. Sorghum vulgare
15. Pennisetum typhoides
16. Acacia arabica
17. Artemisia vulgaris
18. Triticum sativum
19. Avena sativa
20. Brassica nigra
21. Parthenium hysterophorous
22. Cassia siamea
23. Cassia occidentalis
24. Cenchrus barbatus
25. Chenopodium murale
26. Eucalyptus spp
27. Ipombea sp
28. Rumex dentatus
29. Dodonaea viscosa
30. Salvadora Persica
31. Asphodelus tenuifolius
32. Ailanthus excelsa
33. Carica papaya

B. INSECTS

34. Coakroach
35. House fly
36. Grasshopper
37. Mosquito

C. ANIMAL-EPITHELIA

38. Dog-epithelia
39. Pigeon's feather
40. Cat epithelia
41. Sheep's wool

D. DUSTS

42. House dust
43. Cotton dust
44. Hay dust
45. Wheat flour
46. Paper dust

E. FUNGI

47. Aspergillus fumigatus
48. Cladosporium herbarum
49. Candida albicans
50. Penicillium spl.
51. Fusarium solani
52. Aspergillus niger.
53. Alternaria alternata
54. Curvularia lunata
55. Aspergillus flavus
56. Rhizopus nigricans
57. Aspergillus tamarii

F. MITES

58. Mite (D.farinae)
59. Mite (D.pteronyssinus)

G. FOODS

60. Egg (Whole)
61. Milk
62. Prawn
63. Wheat
64. Rice
65. Peanut(Groundnut)
66. Salmon
67. Tomato
68. Banana
69. Lemon
70. Pea
71. Potato
72. Chicken
73. Mutton
74. Crab
75. Pineapple
76. Dal arhar
77. Dal urad
78. Bajra
79. Jowar
80. Moog dal
81. Masoor dal
82. Gram Kabuli
83. Gram bengali
84. Maize

H. 85. Histamine
86. Saline

ANNEXURE- III

TREATMENT RECORD

DESENSOL AQUEOUS ALLERGEN EXTRACTS

Patient's Name : Ref. No. :

Doctor's Name :

Composition :

INITIAL TREATMENT

DOSAGE SCHEME/GUIDELINES:

Vial/ strength	Very sensitive patients (ml)	Moderately sensitive patients (ml)	Date	Individual dosage(ml) Subcutaneous injections	Re mar ks
1	0.05	0.05			
1+24999 Black label	0.10	0.10			
	0.15				
	0.20	0.20			
	0.25				
	0.30	0.30			
	0.35				
	0.40	0.40			
	0.45				
	0.50	0.50			
2	0.05	0.05			
1+2499 Green label	0.10	0.10			
	0.15				
	0.20	0.20			
	0.25				
	0.30	0.30			
	0.35				
	0.40	0.40			
	0.45				
	0.50	0.50			

Vial/ Strength	Very sensitive patients Doses in ml	Moderately sensitive patients Doses in ml	Date	Individual dosage(ml) Subcutaneous injections	Remarks
3	0.05	0.05			
1+249	0.10	0.10			
Blue label	0.15	0.15			
	0.20	0.20			
	0.25	0.25			
	0.30	0.30			
	0.35	0.35			
	0.40	0.40			
	0.45	0.45			
	0.50	0.50			
4	0.05	0.05			
1+49	0.10	0.10			
Red label	0.15				
	0.20	0.20			
	0.25				
	0.30	0.30			
	0.35				
	0.40				

MAINTENANCE THERAPY

Vial/ Strength	Individual dosage(ml) Subcutaneous injections	Date	Remarks
4			
1 + 49			
Red label			